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Atty. Dkt. No. 035394-0117
2186

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Nicolas Voute et al.

Title: SMALL DENSE MICROPOROUS SOLID SUPPORT MATERIALS,
THEIR PREPARATION, AND USE FOR PURIFICATION OF LARGE
MACROMOLECULES AND BIOPARTICLES

Appl. No.: 09/274,014

Filing Date: 03/22/1999

Examiner: D. Sorkin

Art Unit: 1723

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TRANSMITTAL COVER SHEET

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Transmitted herewith is an amendment in the above-identified application.

- [X] Request for Oral Hearing Under 37 C.F.R. § 1.194(b)(1 page).
- [X] Reply to Examiner's Answer, in triplicate (8 pages each).
- [X] Check No. 37396 in the amount of \$290.00 is enclosed for this Request For Oral Hearing fee (37 C.F.R. §1.17(d)).
- [X] The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith,

applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Please direct all correspondence to the undersigned attorney or agent at the address indicated below.

Respectfully submitted,

Steve A. Bent

By Reg. No. 48,571

Date 26 July 2004
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Nicolas Voute et al.

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REQUEST FOR ORAL HEARINGCommissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Under the provisions of 37 C.F.R. §1.194(b), appellant requests an oral hearing.

The item(s) checked below are appropriate:

[X] This request is timely because it is being made within two months from the date of the Examiner's Answer.

[X] The fee of \$290.00 for this Request For Oral Hearing (37 C.F.R. §1.17(d)) is enclosed.

[X] The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 19-0741.

Respectfully submitted,

Stephen A. Bent

Reg. No. 48,571

Date 26 July 2004

By _____

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE HONORABLE BOARD OF PATENT APPEALS AND
INTERFERENCES

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JUL 29 2004

Technology Center 2100

In re the Application of Nicolas VOUTE *et al.*

Application No.: 09/274,014

Filed: March 22, 1999

Docket No.: 035394/0117

For: SMALL DENSE MICROPOROUS SOLID SUPPORT MATERIALS, THEIR
PREPARATION, AND USE FOR PURIFICATION OF LARGE
MACROMOLECULES AND BIOPARTICLES

REPLY TO EXAMINER'S ANSWER

Appeal from Group 1723

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I. SUMMARY OF THE ARGUMENT

The examiner erred by relying on a theoretical calculation for porosity. Furthermore, the examiner dismissed out of hand the unexpected properties of the claimed supports. Looking only to the porosity of prior-art supports, the examiner failed to note other distinctions, already advanced by appellants, that separate the claimed invention from the prior art. There also is no objective evidence of record that one skilled in the art would have been motivated to combine the teachings of Girot and Davis. In any event, moreover, the combination of Girot and Davis would not have foretold the claimed supports.

II. ARGUMENT

Initially, appellants reiterate that the claimed supports differ markedly from those disclosed by Girot. The former possess (i) pore volumes that are less than 30% of the total volume of the mineral oxide matrix and (ii) an interactive polymer network that fills the pores and is coated on the surface of the mineral oxide matrix; as a consequence, interaction with biomolecules occurs on the external surface area of the support. Appellants designed the supports to have low pore volumes and external interaction sites to allow for chromatographic separation of large macromolecules, such as plasmids.

By contrast, Girot discusses chromatographic supports, possessing high sorptive capacity and high porosity, for which interaction with biomolecules occurs within the pores. While Girot's supports are useful for separating small molecules, they are incapable of separating macromolecules, which are too large to enter the pores, from smaller contaminants.

A. The examiner erred by relying on a theoretical calculation for porosity and dismissing out of hand the unexpected properties of the claimed supports

In his Answer, the examiner questions for the first time appellants' method of calculating porosity and provides an alternative calculation. Examiner's Answer, pg. 7, ¶2 to pg. 10, ¶1. With a new formula in hand, the examiner contends that Girot (U.S. patent No. 4,445,732) discloses supports with a porosity ranging from about 30% to about 81% (corresponding to 0.2 to about 2 cm³/g). Based on this understanding, he asserts that Girot renders the claimed supports obvious. Examiner's Answer, pg. 9 to pg. 10.

First, appellants assert that Girot fails to disclose supports having a range of porosities that abuts the porosity range of the claimed supports. While the examiner's method of calculating porosity may be correct from a purely theoretical perspective, empirical studies by appellants have shown that Girot's supports possess, at the lowest end of the range, a porosity of about 40%. Thus, appellant's maintain the position voiced in the Appeal Brief, namely that the person of ordinary skill would *not* have been motivated to extend the range lower than the endpoint of the disclosed range. Such an extension, beyond the range disclosed in Girot ('732), would directly contravene the ability to have biomolecules diffuse into the pores. A porosity of less than 30% as presently claimed is therefore not a "workable" range when considered in light of the purpose of Girot ('732), and one of ordinary skill in the art would not have been motivated to use a pore volume less than the endpoint of Girot's range.

Second, if one assumes, *arguendo*, that Girot discloses supports with a range of porosities that abuts the porosity range of the claimed supports, a finding of obviousness still is precluded, in view of the evidential record, as a matter of law. In wielding his new calculations, the examiner relies on *In re Woodruff*, 919 F.2d 1575 (Fed. Cir. 1990), for the proposition that the prior-art renders the claimed supports *prima facie* obvious. Examiner's Answer, pg. 10, ¶3. The court noted in *Woodruff*, however, that a *prima facie* case of obviousness can be overcome by showing the recited range achieves unexpected results. 919 F.2d at 1578.

In this regard, the examiner here fails to note distinctions, already advanced by appellants, that separate the claimed invention from the prior art. Furthermore, the examiner overlooks properties of the claimed supports that neither Girot nor any cited reference presages. Accordingly, the rationale elaborated in the Examiner's Answer is erroneous as a matter of law.

As noted previously, the inventive supports differ markedly from those of Girot. In particular, the interactive polymer network of the claimed supports fills the pores and is coated on the surface of the mineral oxide matrix so that subsequent interaction with macromolecules occurs on the external surface area of the support. In contrast, Girot's supports interact with biomolecules within the pores. *See e.g.* U.S. patent No. 4,445,732, col. 19, ln. 32 to col. 20, ln. 16.

In addition, the design and mechanism of the inventive supports are substantially different from those disclosed by Girot. The chromatographic supports that Girot describes possess high sorptive capacity and high porosity, and they interact with biomolecules within

their pores. *See, e.g.*, col. 1, ln. 12-29; col. 18, ln. 45-63; and col. 19, ln. 32 to col. 20, ln. 16. The pores of Girot's supports are filled with (i) a thin passivating layer and (ii) a polymer network that forms a lattice within the porous volume. *See, e.g.*, col. 18, ln. 45-63; col. 19, ln. 32-55; and Figure 5. Exemplary supports possess porosities, using the examiner's calculations, of 69 % ($1 \text{ cm}^3/\text{g}$) and 78% ($1.6 \text{ cm}^3/\text{g}$), respectively. *See Examples 1-25.* According to Girot, the polymer network enhances the sorptive capacity of the supports by enhancing diffusion of biomolecules into the pores where they can interact the sorptive groups. *See, e.g.*, col. 19, ln. 44 to col. 20, ln. 16.

Thus, an artisan venturing outside of Girot's suggested porosity range would not have expected to obtain a dense mineral oxide solid support that interacts with macromolecules on its external surface area due to having a pore volume that less than 30 % of the total volume of the mineral oxide matrix and an interactive polymer network that fills the pores and is coated on the surface of the mineral oxide matrix. In contrast to Girot's supports, moreover, the inventive supports exhibit high density, low porosity, and high external surface area.

In sum, the range of pore volumes recited in the instant claims achieved unexpected results. More specifically, pore volumes in the range selected by appellants, because they result in a smaller accessible volume to solutes, allow the rapid separation of large macromolecules, such as plasmids, from smaller molecules in a solution. In contrast, the large pore volumes described by Girot are not useful for this purpose. Girot's supports provide a large accessible, internal surface area which is useful for small molecule separation but which significantly retards separation of large macromolecules. Therefore, the pore volume range selected by appellants is not a mere extension of the range described by Girot. To the contrary, the range of pore volumes recited in the instant claims achieved unexpected results, an outcome characterized by the *Woodruff* court as sufficient to overcome a *prima facie* case of obviousness. By dismissing these unexpected results out of hand, the examiner has committed a legal error.

Accordingly, the appealed rejection under §103 should be overruled.

B. The record is devoid of any "objective evidence" that an artisan would have been motivated to combine the teachings of Girot and Davis

The examiner alternatively asserts that the combination of Girot and Davis renders the claimed supports obvious. This assertion, too, is erroneous as a matter of law.

In levying an obviousness rejection under 35 U.S.C. 103, the examiner has the burden of establishing (1) some suggestion or motivation to modify the reference or to combine reference teachings, (2) a reasonable expectation of success, and (3) that the prior art references, when combined, teach or suggest all the claim limitations. *See MPEP §2143* (May 2004). "Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure." *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438 (Fed. Cir. 1991).

The Federal Circuit often has emphasized the importance of evidencing the requisite motivation to combine references when rejecting claims based upon obviousness. For example, *In re Lee*, 277 F.3d 1338 (Fed. Cir. 2002) (copy appended) dealt with a PTO Board decision that it was unnecessary for the examiner to have presented a source of a teaching, suggestion, or motivation to combine the cited references. At the outset, the court noted that:

The conclusion of obviousness may be made from common knowledge and common sense of a person of ordinary skill in the art without any specific hint or suggestion in a particular reference.

277 F.3d at 1341 (referencing Board op. at 7). The Federal Circuit reversed the Board's decision, observing that,

When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness. *See, e.g., McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1351-52, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001) ("the central question is whether there is reason to combine [the] references," a question of fact drawing on the *Graham* factors).

Id., at 1343. Further, the court stated:

"The factual inquiry whether to combine references must be thorough and searching." *Id.* It must be based on objective evidence of record. This precedent has been reinforced in myriad decisions, and cannot be dispensed with. *See, e.g., Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1124-25, 56 USPQ2d 1456, 1459 (Fed. Cir. 2000) ("a showing of a suggestion, teaching, or motivation to combine the prior art references is an 'essential component of an obviousness holding'") (quoting *C.R. Bard, Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1352, 48 USPQ2d 1225, 1232 (Fed. Cir. 1998)); *In re Dembicza*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."); *In re Dance*, 160 F.3d 1339, 1343, 48 USPQ2d 1635,

1637 (Fed. Cir. 1998) (there must be some motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant); *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) ("teachings of references can be combined only if there is some suggestion or incentive to do so.") (emphasis in original) (quoting *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984)).

Id. See also MPEP §2143 (May 2004, pg. 2100-130))

In the instant case, the examiner attempts to find the requisite motivation in Girot's observation that a "variety of non-passivated porous solid matrices are amenable to passivation by the general method of the present invention," with Girot's identification of zirconium in a list of possible porous matrices. *See* Examiner's Answer, pg. 5, ln. 2-4; pg. 6, ln. 16-20. The examiner asserts that Girot's plan to use "'mineral oxide' matrices including oxides of 'zirconium'" would have "provid[ed] strong motivation [to] look toward the teachings of Davis ('772), which concern zirconium oxide matrices." *See* Examiner's Answer, pg. 5, ln. 5-7. This assertion is erroneous as a matter of law, however, as it fails to provide the requisite motivation to combine, as articulated in *Lee* and its predecessors.

The examiner cites no objective evidence of record that an artisan would have been motivated to combine the chromatographic supports of Girot with the teachings of Davis, which disclosed methods of fabricating sintered zirconia ceramics for use as insulating refractory and catalyst supports. Instead, the examiner attempts to qualify for obviousness purposes every published document referencing zirconium oxide based solely on Girot's listing of possible matrices. This attempt falls well-short of evincing the requisite motivation for combining references, however. Indeed, under the examiner's logic, Girot's generalizations would qualify, for obviousness purposes, the entire published literature associated with non-passivated porous solid matrices.

Accordingly, the examiner has failed to establish a *prima facie* case of obviousness, and the appealed rejection under §103 should be reversed.

C. *The combination of Girot and Davis would not have foretold the claimed supports*

If one assumes, *arguendo*, that an artisan would have been motivated to combine the teachings of Girot and Davis, the artisan still would not have expected to obtain the claimed supports. The design and mechanism of the inventive supports are substantially different from those disclosed by Girot and Davis. Girot talked of chromatographic supports,

possessing high sorptive capacity and high porosity, wherein macromolecular interaction occurs within the pores. In a wholly unrelated context, Davis disclosed methods of fabricating sintered zirconia ceramics for use as insulating refractory and catalyst supports.

To the skilled artisan, therefore, Girot and Davis would not have implicated a dense mineral oxide solid support that interacts with macromolecules on its external surface area, by virtue of having a pore volume that is less than 30% of the total matrix volume and an interactive polymer network that fills the pores and coats the matrix surface. In contrast to prior-art supports, moreover, the inventive supports exhibit high density, low porosity, and high external surface area. By propounding an obviousness analysis that ignores these unexpected properties and results, the examiner has committed reversible error.

For these reasons and for the reasons set out in the main brief, appellants renew their request that the Board overrule the final §103 rejection.

Respectfully submitted,



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26 July 2004
Date

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